Claims

1. An epitope for binding integrins, comprising strands A and G of domain 1 of ICAM-4 (SEQ ID NO: 1), in which the A strand (SEQ ID NO: 2) is defined by amino acid residues 17 to 27 of ICAM-4 and the G strand (SEQ ID NO: 3) is defined by amino acid residues 90 to100 of ICAM-4, or a functional homologue of the epitope.

2. The epitope according to claim 1, defined by amino acid residues F18, W19, V20 on the A strand of ICAM-4 and amino acid residues R92, A94, T95, S96 and R97 on the G strand of ICAM-4.

3. The epitope according to either of claim 1 or claim 2, modified in that the A strand is replaced by strand F on domain 1 of ICAM-4, in which the F strand (SEQ ID NO: 4) is defined by amino acid residues 77 to 87 of ICAM-4.

4. The epitope according to claim 3, defined by amino acid residues W77 and L80 on the F strand of ICAM-4 and amino acid residues R92, A94, T95, S96 and R97 on the G strand of ICAM-4.

5. The epitope according to any preceding claim, further defined by amino acid residues W66 on the E strand of domain 1 of ICAM-4 and K118 on the B strand of domain 2 of ICAM-4, in which the E strand (SEQ ID NO: 5) is defined by amino acid residues 160 to 170 of ICAM-4 and the B strand (SEQ ID NO: 6) is defined by amino acid residues 116 to 126 of ICAM-4.

6. The epitope according to any preceding claim, further defined by amino acid residues N160, V161 and T162 on the E strand of ICAM-4.

7. The epitope according to any preceding claim, in which the integrins are α_v integrins (for example, as found on HT1080 cells), $\alpha_4\beta1$ (also known as VLA-4; for example, as found on HEL cells and erythroblasts), or $\alpha_5\beta1$ (for example, as found on erythroblasts).

8. A footprint domain for binding integrins, comprising a first epitope as defined in any of claims 1 to 6 and a second epitope comprising the C and F strands of domain 1 of ICAM-4 and the CE loop of domain 2 of ICAM-4, in which the C strand (SEQ ID NO: 7) is defined by amino acid residues 47 to 54 of ICAM-4, the F strand (SEQ ID NO: 4) is defined by amino acid residues 77 to 87 of ICAM-4 and the CE loop (SEQ ID NO: 8) is defined by amino acid residues 150 to 158 of ICAM-4, or a functional homologue of the footprint domain.

9. The footprint domain according to claim 8, in which the second epitope is defined by amino acid residues R52 on the C strand of ICAM-4, W77 and L80 on the F strand of ICAM-4, T91, W93 and R97 on the G strand of ICAM-4, and E151 and T154 on the C'-E loop of ICAM-4.

10. The footprint domain according to either of claim 8 or claim 9, in which the integrin ligands are α_v integrins (for example, as found on HT1080 cells), VLA-4 (for example, as found on HEL cells) and/or the β_2-family of integrins (such as Mac-1, for example, as found on leucocytes and on neutrophils, and/or LFA-1), including $\alpha L\beta 2$ (for example, as found on neutrophils).

11. An antagonist of the epitope of claims 1 to 7 and/or the footprint domain of claims 8 to 10.

12. An antagonist of a ligand for the epitope of claims 1 to 7 and/or the footprint domain of claims 8 to 10.

13. The antagonist of claim 12, having or consisting essentially of three, four, five, six, seven, eight, nine or more amino acid residues of the A, C, F or G strands or the CE loop of ICAM-4, or a functional homologue thereof.

14. The antagonist of claim 14, in which the antagonist has or consists essentially of the amino acid sequence according to SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11.

15. A method of antagonising the epitope of claims 1 to 7 and/or the footprint domain of claims 8 to 10, comprising the step of contacting the epitope and/or the footprint domain with the antagonist of claim 11.

16. A method of antagonising a ligand of the epitope of claims 1 to 7 and/or the footprint domain of claims 8 to 10, comprising the step of contacting the ligand with the antagonist of any of claims 12 to 14.

17. Use of the antagonist of any of claims 11 to 14 for treating a disease.

18. The use according to claim 17, in which the disease involves ICAM-4.

19. Use of the antagonist according to any of claims 11 to 14 in the manufacture of a medicament for the treatment of a disease involving ICAM-4.

20. The use according to any of claims 17 to 19, in which disease is characterised by increased levels of ICAM-4 binding.

21. The use according to any of claims 17 to 19, in which the disease is characterised by decreased levels of ICAM-4 binding.

22. The use according to any of claims 17 to 21, in which the disease is sickle cell disease, deep vein thrombosis (DVT), malaria, heart disease, vascular complications, diabetes, β-thalassemia or a thrombotic complication of haematological diseases.

23. An isolated nucleotide encoding the epitope defined in claims 1 to 7 or the footprint domain of claims 8 to 10 or the antagonist of claims 11 to 14.

24. The isolated nucleotide of claim 23, having a sequence defined within the sequence of SEQ ID NO: 12.